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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/046,955	01/14/2002	Christine J. Morrison	6395-62064	5021

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EXAMINER	
GOLDBERG, JEANINE ANNE	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 03/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/046,955	MORRISON ET AL.	
	Examiner	Art Unit	
	Jeanine A Goldberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 January 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7,8,24,30,31,47,49 and 51-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *58 and 59* is/are allowed.

6)☒ Claim(s) *1,7,8,24,30,31,47,49 and 51-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/14/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to the papers filed January 18, 2002.

2. Currently, claims 1, 7-8, 24, 30-31, 47, 49, 51-59 are pending.

Election/Restrictions

3. Applicant's election of Group I, Claims 1, 7-8, 24, 30-31, 47, 49, 51-59 in the reply filed on January 18, 2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Priority

4. The preliminary amendment filed January 14, 2002 has added the priority claim, however the status of the parent application has not been added. The case has been patented as 6,372,430. Insertion of this information is required.

Drawings

5. The drawings are acceptable.

Specification

6. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Claim Rejections - 35 USC § 112- Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1, 7, 8, 24, 30, 31, 47, 49, 55-57 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1, 7-8, 51-54 are indefinite because it is unclear whether the claimed probe does not selectively hybridize to any one of the recited species or whether the claimed probe does not hybridize to all of the recited species. The claims are drawn to "or" and it is unclear whether the claims require that the claimed probe does not hybridize to any of the recited species or whether the claimed probe does not hybridize to one of those species.

B) Claims 7, 8, 24, 30, 31, 47, 49 are indefinite over the recitation "a complentary sequence thereof" because it is unclear whether the claim shares complemntarity with the sequence or whether the sequence is "the complement" such that each of the nucleotides are base paired with the other.

C) Claims 24, 30, 31, 55-57 are indefinite because it is unclear whether the claims are directed to detecting *Fusarium solani* or *Fusarium moniliforme* or whether the claims are drawn to detecting SEQ ID NO: 6 or SEQ ID NO: 7 or whether the claims are drawn to detecting *Fusarium* species more generically as provided in the last line of the claim. It is noted in the art cited below, that SEQ ID NO: 50 is embedded within *Fusarium oxysporum*. Therefore, Claim 56 which is directed to detecting with SEQ ID

NO: 50 would detect not only *Fusarium solani* or *Fusarium moniliforme* but also at least *Fusarium oxysporum*. Thus, detection of SEQ ID NO: 50 would detect a species of *Fusarium* which was not one of "the *Fusarium* species."

D) Claims 47, 49 are indefinite over the recitation "respectively." It is unclear what "respectively" is referring to. The claim appears to be directed to a probe consisting of SEQ ID NO: 59 or a complementary sequence thereof. It is unclear what the "respectively" is referring to as it does not appear that "respectively" relates back to any particular clause.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1, 47, 51, 53 are rejected under 35 U.S.C. 102(b) as being anticipated by Duggal et al. (Genbank Accession Number U28159, June 1995).

As provided in MPEP 2111.03, "for the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising."

Duggal et al. (herein referred to as Duggal) teaches a nucleic acid from *Fusarium oxysporum* strain DAOM 213391 which is the ITS1, 5.8S and ITS2 region. Duggal teaches a nucleic acid which comprises SEQ ID NO: 50. Positions 338-355 of Duggal are identical to all 18 nucleotides of SEQ ID NO: 50.

With respect to Claim 47, Duggal teaches 15 nucleotides, positions 441-455 which are identical to nucleotides 1-15 of SEQ ID NO: 59 of the instant application. Therefor the probe taught by Duggal consists essentially of, i.e. comprises a complementary sequence of SEQ ID NO: 59. "A" complementary sequence implies there is complementarity between the nucleotides. "The" complement of SEQ ID NO: 59 would be directed to the complement of all of SEQ ID NO: 59.

It is noted that the claims require that the isolated probe does not hybridize to the species listed in the instant claim. Duggal teaches a product comprising SEQ ID NO : 50 which is from *Fusarium*. Hybridization conditions are such that can be manipulated to distinguish from other sequences by the conditions used. Higher or lower stringency conditions may be used to allow or prevent hybridization to particular sequences. Thus, the product of Duggal appears to inherently meet the limitations of the claims.

9. Claims 1, 47, 51, 54 are rejected under 35 U.S.C. 102(b) as being anticipated by Duggal et al. (Genbank Accession Number U38558, November 1995).

As provided in MPEP 2111.03, "for the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or

claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising."

Duggal et al. (herein referred to as Duggal) teaches a nucleic acid from *Fusarium solani* which is the ITS1, 5.8S and ITS2 region. Duggal teaches a nucleic acid which comprises SEQ ID NO: 51. Positions 418-438 of Duggal are identical to all 20 nucleotides of SEQ ID NO: 51.

With respect to Claim 47, Duggal teaches 15 nucleotides, positions 463-477 which are identical to nucleotides 1-15 of SEQ ID NO: 59 of the instant application. Therefor the probe taught by Duggal consists essentially of, i.e. comprises a complementary sequence of SEQ ID NO: 59. "A" complementary sequence implies there is complementarity between the nucleotides. "The" complement of SEQ ID NO: 59 would be directed to the complement of all of SEQ ID NO: 59.

It is noted that the claims require that the isolated probe does not hybridize to the species listed in the instant claim. Duggal teaches a product comprising SEQ ID NO : 51 which is from *Fusarium solani*. Hybridization conditions are such that can be manipulated to distinguish from other sequences by the conditions used. Higher or lower stringency conditions may be used to allow or prevent hybridization to particular sequences. Thus, the product of Duggal appears to inherently meet the limitations of the claims.

10. Claims 1, 7-8, 24, 30-31, 47, 49 are rejected under 35 U.S.C. 102(b) as being anticipated by Ligon et al. (WO 95/29260, November 1995).

As provided in MPEP 2111.03, "for the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising."

Ligon teaches detection of fungal pathogens using PCR. Ligon teaches a primer to *Fusarium spp.* (JB572) AAGTTGGGGTTTAACGGC (SEQ ID NO: 59 of Ligon). The primer is a species-specific primer (page 14-15). The alignment provided in Figure 3 illustrates alignment of the ITS sequences from *Fusarium graminearum, Fusarium culmorum, Fusarium moniliforme* and *Micodochium nivale*. The JB572 primer of Ligon is located in a region which is conserved among *Fusarium graminearum and Fusarium culmorum.* The primer is located in a region which contains variability from *Micodochium nivale*. Therefore, the primer which is 19 nucleotides in length is specific for Fusarium and would hybridize to SEQ ID NO: 6 and SEQ ID NO: 7, for example. Moreover, based upon the broad claim language "a complementary sequence," it is clear that the claim does not require the complement. The primer would not hybridize to at least one of the listed genus/species. It is noted that the claims require that the isolated probe does not hybridize to the species listed in the instant claim.

Ligon teaches a product comprising SEQ ID NO : 59 which is from *Fusarium graminearum and Fusarium culmorum*. Nucleotides 456-474 of SEQ ID NO: 82 from Lignon are 100% identical to nucleotides 1-18 of SEQ ID NO: 59 from the instant application. Hybridization conditions are such that can be manipulated to distinguish from other sequences by the conditions used. Higher or lower stringency conditions

may be used to allow or prevent hybridization to particular sequences. Thus, the products of Ligon appears to inherently meet the limitations of the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 56-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ligon et al. (WO 95/29260, November 1995) in view of either Duggal-2 et al. (Genbank Accession Number U38558, November 1995) or Duggal-1 et al. (Genbank Accession Number U28159, June 1995) and further in view of Hogan (US Pat. 5,595,874, Jnauary 1997.)

Ligon teaches detection of fungal pathogens using PCR. Ligon teaches that the ITS sequences are particularly suitable for the detection of specific pathotypes of different fungal pathogens. Ligon teaches that "once the ITS DNA sequence of a pathogen have been determined, they can be aligned with other ITS sequence"(page 6, lines 6-9). Primers can be derived from the ITS sequences and designed based on regions within the ITS regions that contain the greatest difference in sequence among the fungal pathotypes. These sequences and primers based on these sequences can be sued to identify specific pathogen members (page 6, lines 10-12). Ligon teaches comparing ITS sequences to locate divergences which might be useful to test in PCR to distinguish the different species and/or strains (page 7, lines 14-16). Ligon teaches various conditions which can be varied to obtain hybridization. Ligon teaches using regions with the greates differences among species and also to the highest homology within genus depending on the objective of the detection. Ligon teaches a primer to *Fusarium spp.* (JB572) AAGTTGGGGTTTAACGGC (SEQ ID NO: 59 of Ligon). The primer is a species-specific primer (page 14-15). The alignment provided in Figure 3 illustrates alignment of the ITS sequences from *Fusarium graminearum, Fusarium culmorum, Fusarium moniliforme* and *Micodochium nivale*. The JB572 primer of Ligon is located in a region which is conserved among *Fusarium graminearum and Fusarium culmorum.* The primer is located in a region which contains variability from *Micodochium nivale*. Therefore, the primer which is 19 nucleotides in length is specific for *Fusarium* and would hybridize to SEQ ID NO: 6 and SEQ ID NO: 7, for example. Moreover, based upon the broad claim language "a complementary sequence," it is

clear that the claim does not require the complement. The primer would not hybridize to at least one of the listed genus/species. It is noted that the claims require that the isolated probe does not hybridize to the species listed in the instant claim.

Duggal-2 et al. (herein referred to as Duggal) teaches a nucleic acid from *Fusarium solani* which is the ITS1, 5.8S and ITS2 region. Duggal teaches a nucleic acid which comprises SEQ ID NO: 51. Positions 418-438 of Duggal are identical to all 20 nucleotides of SEQ ID NO: 51.

Duggal-1 et al. (herein referred to as Duggal) teaches a nucleic acid from *Fusarium oxysporum* strain DAOM 213391 which is the ITS1, 5.8S and ITS2 region. Duggal teaches a nucleic acid which comprises SEQ ID NO: 50. Positions 338-355 of Duggal are identical to all 18 nucleotides of SEQ ID NO: 50.

Moreover, Hogan et al. (herein referred to as Hogan) teaches the use of specific primers col. 6-7, lines 50-67, lines 1-12, and furthermore provides specific guidance for the selection of primers,

> "Once the variable regions are identified, the sequences are aligned to reveal areas of maximum homology or 'match'. At this point, the sequences are examined to identify potential probe regions. Two important objectives in designing a probe are to maximize homology to the target sequence(s) (greater than 90% homology is recommended) and to minimize homology to non-target sequence(s) (less than 90% homology to non-targets is recommended). We have identified the following useful guidelines for designing probes with the desired characteristics.
> First, probes should be positioned so as to minimize the stability of the probe:nontarget nucleic acid hybrid. This may be accomplished by minimizing the length of perfect complementarity to non-target organisms, avoiding G and C rich regions of homology to non-target sequences, and by positioning the probe to span as many destabilizing mismatches as possible (for example, dG:rU base pairs are less destabilizing than some others). Second, the stability of the probe:target nucleic acid hybrid should be maximized. This may be accomplished by avoiding long A and T rich sequences, by terminating the

> hybrids with G:C base pairs and by designing the probe with an appropriate Tm. The beginning and end points of the probe should be chosen so that the length and %G and %C result in a Tm about 2-10°C higher than the temperature at which the final assay will be performed. The importance and effect of various assay conditions will be explained further herein. Third, regions of the rRNA which are known to form strong structures inhibitory to hybridization are less preferred. Finally, probes with extensive self complementarity should be avoided."

Therefore, it would have been prima facie obvious to one of ordinary skill at the time the invention was made to have modified the genus and species specific PCR primers taught by Ligon using the alignment, teachings of additional Fusarium species of Duggal-1 and -2 and the specific guidance provided by Hogan to obtain the invention as a whole. The primers of Ligon are located in the same region, namely the ITS2 region, as SEQ ID NO: 50, 51, 59, for example. Given the teachings in the art directed to modifying probes and primers to obtain functional equivalents, the ordinary artisan would have been motivated to have selected any other probe or primer which would function to detect and discriminate *Fusarium solani* from other *Fusarium* species. At the time the invention was made it was routine to take ITS2 sequences from fungal species, align the sequence and design probes/primers which had high homology for genus specific primers or which had species specificity. The state of the art was such that designing probes which hybridized to specific regions was well developed. Both Ligon and Hogan teach the ordinary artisan how to select specific probes and primers which may be used in species specific or genus specific manner depending on the needs of the assay. Moreover, at the time the invention was made, the sequence of the *Fusarium* species nucleic acids of distinct types were known and it would have been

prima facie obvious to one of ordinary skill in the art at the time the invention was made and within the skill of the art to obtain the instantly claimed oligonucleotides following the teachings of Ligon and Hogan as to the identification of sequences that are genus specific and thus useful for the identification of *Fusarium* species by hybridization. Further, the teachings of the art indicate that the state of the art at the time the invention was made would have led one of ordinary skill in the art to the claimed genus-specific probes because Ligon, Duggal-1, Duggal-2 and Hogan teaches the usefulness of the ITS2 region of the *Fusarium* species for species-specific probes, species-specific primers and further teaches methods in which the probes may be modified. SEQ ID NO: 50 and 51 are located in regions which are not conserved among Fusarium species. Thus, the ordinary artisan would have been motivated to have used either of these sequences for the detection of particular Fusarium species.

Allowable Subject Matter

13. The prior art fails to teach or suggest "an isolated nucleic acid sequence comprising SEQ ID NO: 6 or SEQ ID NO: 7." Claims 58 and 59 are drawn to an isolated nucleic acid sequence comprising SEQ ID NO: 6 or 7 and an isolated nucleic acid sequence consisting essentially of SEQ ID NO: 6 or 7.

Conclusion

14. No claims allowable.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (571) 272-0743. The examiner can normally be reached Monday-Friday from 7:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272- 0745.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

J. Goldberg

Jeanine Goldberg
Patent Examiner
March 7, 2005